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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,295	PAUL, SUDHIR	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-25 and 27-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6-25 and 27-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to comply*.

DETAILED ACTION

1. This Office action is in response to the amendment filed November 30, 2009. Claims 3-5 and 26 have been cancelled. Claims 1, 2, 6-25 and 27-50 are pending, and are considered in this Office action.

Specification

2. The objection to the specification for containing an embedded hyperlink and/or other form of browser-executable code **is withdrawn** in view of the amendment to the specification.

3. The amendment to the specification, filed on November 30, 2009, to include SEQ ID NO: in the sequences presented in the specification, is acknowledged.

Drawings

4. The replacement sheets of Figure 2, 5B, 10A, 10B and 10C, filed on November 30, 2009, is acknowledged.

Sequence Rule

5. **(New objection)** It is noted that the specification has failed to submit a sequence list. See attached Notice to Comply.

Claims Objections

6. **(Prior objection-withdrawn)** The objection to Claims 1 and 2 for some informalities is withdrawn in view of the amendment to the claims.

7. **(New Objection)** It is suggested to replace the term "a purified attenuated mutant" of Claims 1, 2, 6-25 and 27-50 by the term "an isolated antibody fragment" or "a purified antibody fragment". The examiner regrets the typographic error in Para 13, the Office action dated May 21, 2009.

Note: For the purpose of examination and to be consistent with the specification, the term "a purified attenuated mutant thereof" in the amended Claims 1, 2, 6-25 and 27-50 is interpreted as "a purified antibody fragment thereof".

Claim Rejections - 35 USC § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 USC 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. **(Prior rejection-withdrawn)** The rejection of Claims 36, 40 and 50, for referring HERV sequences to the GenBank accession number rather than to sequences set forth in the specification, **is withdrawn** in view of amendment to the claims.

Claim Rejections - 35 USC § 101 Utility

10. 35 USC 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. **(Prior rejection-withdrawn)** The rejection of Claims 1-7, 15, 26-28 and 47-50 under 35 USC 101, for being directed to non-statutory subject matter, **is withdrawn** in view of the amendment of the claims.

Claim Rejections - 35 USC § 112, first paragraph

12. The following is a quotation of the first paragraph of 35 USC 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. **(Prior rejection-maintained)** The rejection of Claims 1, 2, 6-25 and 27-50 under 35 USC 112, first paragraph, for failing to comply with written description requirement, **is maintained** for the reason of record.

In response to Applicant's argument:

14. Applicant argues that the specification has a description for the claimed antibody to HIV because it has disclosed a few antibody fragments, which recognize residues 421-436 of HIV gp120 (CD4 binding site) and HIV.

15. This argument is considered, but found not persuasive. As indicated the previous Office action, one species of antibody disclosed by the specification is not a sufficient number of representative species for the claimed subgenus of antibodies. See Para 17 and 18, the office action dated May 21, 2009. The rejection is therefore maintained.

16. **(New rejection-necessitated by the amendment)** Claims 1, 2, 6-25 and 27-50 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

17. Please note that the subject matter of the newly amended Claims 1, 3-5, 10 and

11, "A non-catalytic, non-chimeric monoclonal antibody...", is a NEW MATTER. A survey of the specification has failed to find support for the exclusion of any antibodies having catalytic property or any modified (chimeric) antibodies in the specification as originally filed. Removal of all new matter is required. See In re Russsmussen 210 USPQ 325.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 USC 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. **(Prior rejection-withdrawn)** The rejection of Claims 1-8, 15-23, 26-29, 38, 39 and 47- 49 under 35 USC 102(b) as being anticipated by Paul, *et al.* (6,156,541, cited in IDS), as evidenced by Gorny MK *et al.* (J. Virology, 76(18):9035-9045), **is withdrawn** in view of the amendment to the claims. The claims have been amended to being directed to "a non-catalytic monoclonal antibody", whereas the cited reference teaches catalytic antibodies. The rejection is therefore withdrawn.

102/103 REJECTION

20. **(Prior rejection-maintained)** The rejection of Claims 1, 2, 6-8, 15-23, 27-29, 36-42 and 47-50 under 35 USC 102(b) as being anticipated by or, in the alternative, under 35 USC 103 as being obvious over Chang (US 6,309,880, issued Oct. 30, 2002), as

evidenced by Gorny MK *et al.* (J. Virology, 76(18):9035-9045, 2002), further evidenced by Bost (Immunological Investigations, 17(6&7):577-586, 1988), Golding, H. *et al.* J. Exp. Med., Mar 1988; 167: 914 – 923; and Langat DK, *et al.* (J Reprod Immunol. 1999 Jan;42(1):41-58), **is maintained** for the reason of record.

In response to Applicant's argument:

21. Applicant asserts that Chang teaches chimeric Ab that binds to residues 423-437 of HIV gp120 and neutralizes a single strain of HIV-1. Applicant asserts (1) Chang does not teach any non-chimeric monoclonal antibodies or fragments thereof. (2) Chang's antibodies were obtained by immunization of mice with gp120, not from an autoimmune organism. (3) The sequences of Chang's antibodies are not same as the sequences of the antibodies of the present application. Chang's antibodies do not express the potent and broad neutralization of genetically diverse HIV-1 strains seen with the antibodies of the present invention. Based on this, Applicants submit that Chang teaches away from the instant claimed invention.

22. Applicant's arguments are considered, but found not persuasive. Regarding to Applicant's argument (1), Chang teaches a naturally occurring monoclonal antibody (or produced by hybridoma cell) to HIV gp120, see e.g. Para 1, col. 5; and bridging Para between col. 2 and 3. These monoclonal antibodies are not chimeric antibodies.

23. Regarding to Applicant's argument (2), the previous Office action has provide discussion indicating that the patentability of "product-by-process" claims is determined by the product itself, not by the process, see Para 22, the office action dated May 21, 2009.

24. Regarding to Applicant's argument (3), this argument is not relevant because Applicant is arguing a limitation that is not in the claims. By definition, an antibody is defined by its specificity to a specific antigenic determinant or epitope, see Para 27-33, the Office action dated May 21, 2009. Chang teaches neutralizing antibodies or antibody

fragments that binds epitope IINMWQKVGKAMYAP (SEQ ID NO: 1), corresponding to residues 423-437 of HIV gp120, see e.g. l. 39-52, col. 2; and line 19-25, col. 5. The epitope of SEQ ID NO: 1 shares 100% homology with the HIV antigen epitope used in the instant specification, see Specification, p. 26, line 10-34. See the sequence alignment below:

```
    IINMWQKVGKAMYAP   SEQ ID NO: 1, Chang
KQIINMWQKVGKAMYAP   epitope used to select the claimed Ab
```

Thus, the scope of claims encompasses those antibodies to the same epitope as IINMWQKVGKAMYAP of SEQ ID NO: 1 disclosed by Chang. Importantly, Chang's antibody must inherently recognize and bind or cross-react with the HERV antigen fragment of the instant claim, because the specification teaches that gp120 epitope, IINMWQKVGKAMYAP (SEQ ID NO: 1), shares certain sequence homology with HERV sequence encoded by Genback NO. AL592563.7; see specification, see p. 7 and 8, and Fig. 2 and Table 1. It is noted that Applicant also indicated on the record that the claimed antibody recognized those epitopes which share homogenous sequence with residues 421-436 of gp120, see Remarks, p. 2, in the reply filed August 29, 2008. Thus, Chang's antibody to IINMWQKVGKAMYAP (SEQ ID NO: 1) must recognize and bind the HERV antigen of the instant claims.

25. Since Applicant has not provided evidence showing that the claimed antibody does not have same specificity as that disclosed by Chang, the rejection is maintained.

Claim Rejections - 35 USC § 103

26. The following is a quotation of 35 USC 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. **(Prior rejection-withdrawn)** The rejection of Claims 36, 37, 40, 41 and 50 under 35 USC 103(a) as being unpatentable over Paul S. (6,156,541, '541), as evidenced by Gorny MK *et al.* (J. Virology, 76(18):9035-9045), as applied to Claims 1-8, 15-23, 26-29, 38, 39 and 47-49 above, further in view of Chang (US 6,309,880), Pau S *et al.* (2) (Appl. Biochem Biotechnol. 2000, Jan-Mar; 83(1-3), 00.71-82, cited in IDS), Bost (Immunological Investigations, 17(6&7):577-586, 1988), Golding, H. *et al.* (J. Exp. Med., Mar 1988; 167: 914 – 923); and Langat DK, *et al.* (J Reprod Immunol. 1999 Jan;42(1):41-58), **is withdrawn** in view of the amendment to the claims. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

28. **(New rejection-necessitated by the amendment)** Claims 1, 2, 6-25, 27-35, 38, 39 and 43-49 are rejected under 35 USC 103 as obvious over Chang (US 6,309,880, issued Oct. 30, 2002), Bermas (AIDS Res. and Human Retroviruses, 10(9):1071-1077, 1994) and Gorny MK *et al.* (J. Virology, 76(18):9035-9045, 2002).

29. Chang teaches neutralizing antibodies or antibody fragment that binds epitope IINMWQKVGKAMYAP of SEQ ID NO: 1, corresponding to residues 423-437 of HIV gp120, see e.g. l. 39-52, col. 2; and line 19-25, col. 5. Chang teaches that this epitope is highly conserved among HIV-1 strains and isolates; consequently, an antibody specific for one or more of these epitopes can inhibit diverse strains and isolates of HIV-1, see

e.g. Example 1, col. 9-11.

30. Chang does not teach that the antibody to gp120 is from an organism with autoimmune diseases. Chang does not explicitly teach the antibody fragment is a recombinant single-chain Fv construct.

31. Bermas teaches that antibodies from sera of patients with systemic lupus erythematosus (SLE) have same specificities as antibody to gp120, see e.g. Abstract. Antibodies from sera of SLE patients recognize epitopes of gp120, of which the sequence of T1 epitope share 100% homology with the gp120 epitope of SEQ ID NO: 1 disclosed by Chang, See sequence alignment below.

```
KQIINMWQEVGKAMYA     T1 Bermas
  IINMWQKVGKAMYAP    SEQ ID NO:1 Chang
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32. Gorny teaches that monoclonal antibodies to HIV gp120 show cross-clade binding to native, intact HIV virions of Clades A, B, C, D and F, See e.g. Abstract, and Para 1-2, right col. p. 9042. Thus, the monoclonal antibody against HIV-1 gp120 inherently has ability to neutralize more than two strains of different HIV clades.

33. Kriangkum provides teachings indicating that constructing a single chain Fv is widely used in the art of antibody to enhance antibody function. Specifically, Kriangkum teaches that in single chain Fv constructs, variable domains of heavy and light chains are joined together with a linker to form a single polypeptide chain. Recombinant antibodies have been further altered by genetic fusion with ligands or biologically active molecules resulting in the formation of bifunctional antibodies. Alternatively, fusion of two different antibodies gives rise to the formation of bispecific antibodies; see e.g. right col. p. 31.

34. It would have been obvious to the ordinary artisan to isolate/make an antibody from SLE patients that can recognize and neutralize HIV, as an alternative or an equivalent, for treatment of AIDS as taught by Chang. The skilled artisan would have been motivated to do so, and would have a reasonable expectation of success in obtaining such antibody which cross-reacts with gp120 and HERV antigen, given the knowledge that antibodies in SLE patient can "cross-react" with gp120, as shown by Bermas.

35. The skilled artisan would also have a reasonable expectation of success that such antibody, or antibody fragment, can react with different strains of HIV, given the knowledge that the CD4 binding site of gp120 (a. a. 421-436) IINMWQKVGKAMYAP SEQ ID NO: 1 is highly conserved in HIV strains, as taught by Chang, and also given the knowledge that a gp120 antibody can cross-react with HIV virions of Clades A, B, C, D and F, as taught by Gorny.

36. Finally, the skilled artisan would also have a reasonable expectation of success in making single chain Fv because construction of a single chain Fv is widely used in the art of antibody to enhance antibody function as detailed by Kriangkum. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not

identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

37. (**Prior rejection-withdrawn**) The rejection of Claims 1-10, 15-17, 21, 26-28, 38, 39 and 47-49 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-8 of U.S. Patent No. 6,156,541 ('541), **is withdrawn** in view of the amendment to the claims. The claims have been amended to being directed to "a non-catalytic monoclonal antibody", whereas the '541 teaches catalytic antibodies. The rejection is therefore withdrawn.

Remarks

38. No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE

MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan, Ph.D. can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648